Synthesis of 10-Benzoyl-9-acridone and 9-Acridone from 2,2'- and 2,3'-Disubstituted Benzophenones

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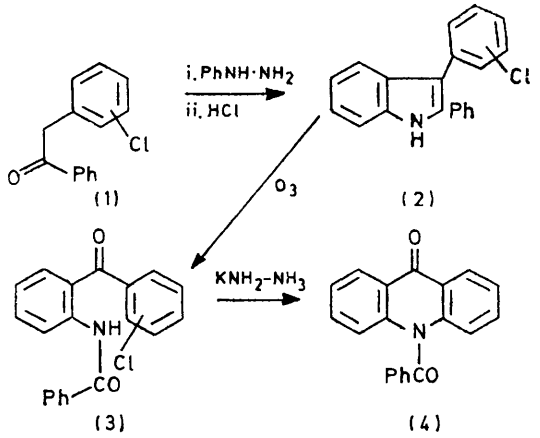
Procedures are described for preparation of 10-benzoyl-9-acridone from 2-benzamido-2'- and -3'-chlorobenzophenones, and of 9-acridone from 2-amino-2'- and -3'-chlorobenzophenones.

ACRIDONES are commonly prepared by cyclization of diphenylamine-2-carboxylic acids under acidic conditions.[1] We now report two syntheses each of 10-benzoyl-9-acridone and of 9-acridone in which the heterocyclic ring is closed under basic conditions (see Scheme).



SCHEME

The ring closures to give 10-benzoyl-9-acridone involved treatment of compounds (3a and b) with potassamide in ammonia. For such ketones, it was thought that competing addition of amide ion to the carbonyl group would be less significant than for *o*- and *m*-chlorobenzophenone, respectively,[2] because of electron delocalisation and, to the extent to which it might occur, would still favour 9-acridone formation *via* the corresponding aryne; similar considerations apply to the amino-ketones prepared by hydrolysis of (3a and b). In the event, treatment with potassamide (8—9 equiv.) gave (4) in 67 and 36% yield, respectively; (3b) gave a second product resulting from external addition of amide ion to an intermediate aryne. It is significant that the *N*-benzoyl group is not removed under these conditions. Surprisingly, 2-amino-2'- and -3'-chlorobenzophenones were recovered (91 and 78%, respectively) from similar treatment; however, conversion into 9-acridone was successfully achieved in both cases by using potassium t-butoxide in refluxing t-butylbenzene.[3]

A number of 2-amino-2'-fluorobenzophenones have been converted into 9-acridones by refluxing with potassium carbonate in dimethylformamide or 2-ethoxyethanol, an *N*-*p*-tolylsulphonyl group being at least partially retained in the latter solvent;[4] choice of conditions is apparently important, since sodium methoxide in toluene converts similar ketones into 2-amino-2'-methoxybenzophenones.[5] Formation of a 9-acridone by elimination of methanol from a 2-amino-2'-methoxybenzophenone has also been reported.[6]

EXPERIMENTAL

Mass spectra were determined with an A.E.I. MS30 spectrometer operating at 70 eV unless otherwise stated. Ozonolyses were performed with a Welsbach T-408 laboratory ozonator: operating voltage, operating pressure, and oxygen flow rate were maintained constant and ozone concentration was determined iodometrically.

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2-(o-*Chlorophenyl*)*acetophenone* (1a).—This ketone, prepared from *o*-chlorophenylacetic acid and benzene,[7] crystallized from light petroleum (b.p. 30—60°) as plates (77%), m.p. 69° (lit.,[8] 70·5°). The mass spectra of compounds (1a and b) [7] show base peaks at *m/e* 105 (PhCO); peaks at *m/e* 232/230 (M^+) were detectable (*ca.* 1%) at 24 eV, but complete cleavage of the molecular ions occurred at 70 eV.

3-(o-*Chlorophenyl*)-2-*phenylindole* (2a).—The ketone (1a) (9·5 g) was treated essentially as described for the analogous *o*-fluoro-compound.[9] Chromatography of the crude product on Florisil and elution with benzene–light petroleum (b.p. 115—120°) (1 : 1) gave the *indole* (2a) (7·6 g, 70%) as plates, m.p. 146—148° (Found: C, 79·0; H, 4·8; Cl, 11·85. $C_{20}H_{14}ClN$ requires C, 79·1; H, 4·6; Cl, 11·7%).

Similarly prepared 3-(m-*chlorophenyl*)-2-*phenylindole* (2b) (49%) formed plates, m.p. 114—115° (from hexane) (Found: C, 78·8; H, 4·55; Cl, 11·8%).

2-*Benzamido*-2′- *and* -3′-*chlorobenzophenones* (3a *and* b).[9]—3-(*o*-Chlorophenyl)-2-phenylindole (10·0 g), dissolved in glacial acetic acid (150 ml), was ozonized for 1·5 h at an ozone flow rate of 1·5 g h^{-1} (*i.e.* 50% excess). The resulting solution was poured into water (150 ml) and after 2 h was extracted with dichloromethane (3 × 50 ml). The extract was washed with aqueous sodium carbonate and water, and was then dried and evaporated. Chromatography of the oily residue (5·6 g) (Florisil; hexane) gave 2-*benzamido*-2′-*chlorobenzophenone* (3a) (4·0 g, 36%) as yellow plates, m.p. 109—110° (Found: C, 71·55; H, 4·05; N, 4·1. $C_{20}H_{14}ClNO_2$ requires C, 71·55; H, 4·15; N, 4·15%); *m/e* 337/335 (M^+), with low intensity peaks at 353/351 presumably due to traces of ozonide.

Similarly prepared, 2-*benzamido*-3′-*chlorobenzophenone* (3b) (42%) formed yellow plates, m.p. 123—124·5° (from hexane) (Found: C, 71·3; H, 4·3; N, 4·45%).

2-*Amino*-2′- and -3′-*chlorobenzophenones*.—Compound (3a) (1·4 g) was refluxed for 4 h with sodium hydroxide (7·5 g) in ethanol (30 ml) and water (10 ml) to give 2-amino-2′-chlorobenzophenone (0·45 g, 40%), yellow plates, m.p. 58—60° (from acetone–hexane) (lit.,[10] 58—60°). Similarly prepared, and purified by chromatography (silica; benzene), 2-*amino*-3′-*chlorobenzophenone* (66%) formed yellow plates, m.p. 78—80° (from hexane) (Found: C, 67·4; H, 4·3; N, 6·0. $C_{13}H_{10}ClNO$ requires C, 67·4; H, 4·3; N, 6·05%).

10-*Benzoyl*-9-*acridone*.—(i) 2-Benzamido-2′-chlorobenzophenone (2·0 g, 0·006 mol), dissolved in dry ether (60 ml), was added to a stirred solution of potassamide [from potassium (2·0 g, 0·051 g atom)] in dry liquid ammonia (200 ml). After 4 h, ammonium chloride (5 g) and ether (50 ml) were added and the ammonia was allowed to evaporate. The residue was treated with 2M-hydrochloric acid (150 ml) and the mixture was extracted with ether; basification of the acidic solution (A) gave (3a) (51 mg) (t.l.c.). The ethereal solution was extracted with aqueous sodium hydroxide; acidification of the alkaline solution (B) and evaporation gave principally inorganic salts. The remaining ethereal solution (C) was washed with water, dried, and evaporated to give a yellow solid, predominantly one compound (t.l.c.). Sublimation at 120° and 15 mmHg gave 10-*benzoyl*-9-*acridone* (4) (1·21 g, 67%) as yellow plates, m.p. 198—200°, identical with the sample from the following experiment.

(ii) 2-Benzamido-3′-chlorobenzophenone (2·0 g) was treated with potassamide in ammonia and the mixture was worked up as in the foregoing experiment. The ethereal solution (C) gave the acridone (4) (0·76 g), m.p. 194—198°, raised to 198—199·5° by chromatography (Florisil; benzene) and crystallization from hexane (Found: C, 80·2; H, 4·6; N, 5·0. $C_{20}H_{13}NO_2$ requires C, 80·5; H, 4·35; N, 4·7%). The final eluates gave tarry material (0·12 g) which was discarded. The acidic solution (A), when basified, gave a yellow compound (0·32 g), m.p. 234—236° (from propan-1-ol); $\nu_{max.}$ (KBr) 3400 (N–H) and 1677 cm^{-1} (C=O); *m/e* 316 (M^+, $C_{10}H_{16}N_2O_2$), probably an amino-benzamidobenzophenone. The basic solution (B), when acidified, gave tarry material (0·42 g).

9-*Acridone*.—(i) 2-Amino-2′-chlorobenzophenone (1·6 g, 0·005 mol), potassium t-butoxide (1·1 g, 0·011 mol), and t-butylbenzene (50 ml) were refluxed with stirring under nitrogen for 12 h. The mixture was concentrated *in vacuo* and the product was collected, washed with water, and dried. Crystallization from ethanol gave slightly impure 9-acridone (1·1 g, *ca.* 78%), m.p. 335—350°, raised to 340—355° by sublimation in *vacuo*.

(ii) 2-Amino-3′-chlorobenzophenone (1·4 g) and potassium t-butoxide (0·82 g), treated as in the foregoing experiment, gave a crude product (0·56 g), m.p. 290—339°. Chromatography (Florisil; benzene) gave 9-acridone (0·41 g, 35%) as yellow needles, m.p. 354—357°, after sublimation *in vacuo*. A second, minor component was not completely freed from 9-acridone and was not identified.

The identity of the two samples of 9-acridone was confirmed by i.r. and mass spectral correlations with an authentic sample.

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